

Urinary tract infections treated with single dose of short-acting sulphonamide

GUNILLA KÄLLENIOUS, JAN WINBERG

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Summary and conclusions

In a prospective study 29 patients with urinary tract infections caused by sulphonamide-sensitive organisms were treated with a single oral dose of the short-acting sulphonamide sulphafurazole. Twenty-seven (93%) of the 29 patients—and possibly all 29—were cured of their infections. There was no difference in the recurrence rates after single-dose treatment and treatment for 10 days or more. Six out of eight strains of *Escherichia coli* causing early recurrences were sensitive to sulphonamides.

These results suggest that uncomplicated infections may safely and successfully be treated by a single oral dose of a short-acting sulphonamide.

Introduction

Although urinary tract infections (UTIs) are common in children, especially girls, no well-documented guidelines exist about how long, how often, and in what doses treatment should be administered. Previously a rapid recurrence of UTI after treatment was thought to be caused by a remaining focus in the urinary tract and, for that reason, long-term treatment was preferred. It is now generally accepted that recurrences in most cases are reinfections with new organisms emanating from the faecal reservoir.¹⁻³ The distinction between prophylaxis and treatment of a current UTI, therefore, must be emphasised. The correct duration of prophylaxis has been the subject of several studies. On the other hand, the minimal time needed to eradicate an acute UTI has not been sufficiently clarified. We undertook this study to see whether a single dose of a short-acting sulphonamide was efficient in eradicating non-febrile UTIs in girls in whom they recurred.

Patients and methods

We investigated 29 girls attending a urinary infection clinic who had a history of repeated symptomatic UTI. Their mean age was 10.4 years (range of 6-14). All had undergone intravenous urography, and none had scarring, stones, or obstruction. Five patients had vesicoureteric reflux grade I or II.⁴ The serum creatinine concentration did not exceed 120 $\mu\text{mol/l}$ (1.4 mg/100 ml), and the renal concentrating capacity was ≥ 800 mmol (mosmol)/l. Patients with temperatures above 38°C or flank pain were not included in the study. The erythrocyte sedimentation rate (ESR) was below 10 mm in the first hour in 28 of the patients. In eight cases a C-reactive protein was obtained and proved negative. These investigations indicated that the infection was confined to the lower urinary tract.

Departments of Paediatrics, Huddinge and Karolinska Hospitals, Karolinska Institutet, S-104 01 Stockholm, and Department of Bacteriology, National Bacteriological Laboratory, S-105 21, Stockholm, Sweden

GUNILLA KÄLLENIOUS, MD, paediatrician
JAN WINBERG, MD, professor

Infection was regarded as definite when two consecutive clean-voided midstream specimens yielded a pure culture of the same organism in a concentration of over 100 000 bacteria/ml of urine. Urinary leucocytes exceeded $50 \times 10^6/\text{l}$ ($50/\text{mm}^3$) uncentrifuged urine in 18 patients.

CLINICAL INVESTIGATIONS

When infection was indicated by a positive urine culture of an organism sensitive to sulphonamide the patient was sent to the clinic, where a second specimen was taken for culture and the urinary leucocyte count and ESR were estimated. Each patient was given 200 mg of sulphafurazole suspension/kg body weight in a single oral dose. Sulphafurazole is a short-acting sulphonamide with a half life of six hours. Morning urine specimens were cultured daily at home during the next seven days using dipslides (Uricult, Orion Diagnostica, Helsinki, Finland); these were later read at the National Bacteriological Laboratory. Fourteen days later quantitative urine culture was performed.

LABORATORY INVESTIGATIONS

Urine specimens were cultured and bacterial counts performed with the standard loop technique. After speciation sensitivity tests were performed by the standardised disc diffusion method and the minimum inhibitory concentration (MIC) determined by the agar dilution method,⁵ using PDM-ASM agar (AB Biodisc, Solna, Sweden).

Serotyping—All *Escherichia coli* were serotyped by determining specific O antigens⁶ and the presence of K antigens.⁷

Biotyping—The API 20E test kit system was used (API System, France). The seven-digit profile was determined twice for all strains, with good reproducibility.

Results

All dipslide cultures performed during the first week showed little or no bacterial growth. At two weeks 10 cultures were positive. In eight of them the infections were caused by new strains or species (table I). Table II shows the results of serotyping and the API profile

TABLE I—Results of treating index infection with one oral dose of sulphafurazole

No of patients treated	29
No of positive cultures at one week	0
No of positive cultures at two weeks	10*
New strains or species	8
Same strain	2
Minimum No of patients cured of index infection	27 (93%)

*Verified by two cultures.

in the index infection and recurrences. In cases 14 and 23 both index infections and recurrences were caused by the same *E coli* strain, as evidenced by the colony morphology, API pattern, and serology. This might indicate a recrudescence of the original infection, but since the recurrences occurred after seven negative dipslides had been obtained more probably they were reinfections. In case 26 the *E coli* strains could not be typed before or after treatment. Their colony morphology and API patterns differed, however, so we assumed that they were different strains. Thus at least 27 (93%) and possibly all of the 29 index infections were cured.

TABLE II—Bacterial aetiology and sensitivity to sulphonamide in 10 patients with early recurrence

Case No	Index infection				Recurrence			
	Species	Sensitivity*	Serotype	API 20E 7-digit profile	Species	Sensitivity*	Serotype	API 20E 7-digit profile
1	<i>Escherichia coli</i>	S	0NKN	0144552	<i>E coli</i>	S	07KI	5144552
2	<i>E coli</i>	S	020KN	5144572	Enterococci	R		
3	<i>E coli</i>	S	02KI	5144552	<i>Staphylococcus epidermidis</i>	ND		
7	<i>E coli</i>	S	0NKI	4144552	<i>E coli</i>	S	021KN	1144572
14	<i>E coli</i>	S	022083KI	5144572	<i>E coli</i>	S	022083KI	5144572
17	<i>E coli</i>	S	013022KN	1044552	<i>E coli</i>	R	0NKN	5144552
19	<i>E coli</i>	S	017077KN	7044573	<i>E coli</i>	R	01KI	5144512
23	<i>E coli</i>	S	0NK3	5144552	<i>E coli</i>	S	0NK3	5144572
26	<i>E coli</i>	S	0NKN	5144572	<i>E coli</i>	S	0NKN	1044552
28	<i>E coli</i>	S	0120KN	1044552	<i>E coli</i>	S	0NKI	5144552

*S = Sensitive (minimum inhibitory concentration < 32 µg/ml). R = Resistant (minimum inhibitory concentration > 1024 µg/ml). ND = Not done.

Table III shows when the infection first recurred after the single-dose treatment. No reinfections occurred during the follow-up period in eight patients, of whom two were followed up for 31-180 days and six for 181 days or more. After the first recurrence patients were treated for 10 days. Management was then tailored to the individual, some patients being given prophylaxis for a longer period. The time lapse from the interruption of treatment or prophylaxis to the next recurrence was recorded. The infection recurred within two months of the interruption of treatment in 12 (71%) out of 17 patients followed up. The corresponding numbers in whom the infection recurred after single-dose treatment were 15 (52%) within two months and 21 (72%) within one year (table III). Thus the shorter treatment did not increase the risk of early recurrence.

TABLE III—Time of appearance of first recurrence after single dose of sulphafurazole

Days after treatment	0-7	8-14	15-30	31-60	61-90	91-180	181-360
Cumulative No of infected patients*		10	12	15	16	17	21

*Each patient represented by only first recurrence.

A selection criterion for this study was that the organisms were sensitive to sulphonamides by conventional disc tests. MICs were less than or equal to 32 µg/ml for all the organisms giving the index infections. Of the re-infecting *E coli* strains, two were resistant (MIC > 1024 µg/ml) while the remaining six were sensitive (MIC < 32 µg/ml) (table II). The remaining two infections were caused by enterococci and *Staphylococcus epidermidis*.

Discussion

In this study 27 out of 29 patients—and possibly all 29—were cured of their infections by a single oral dose of a short-acting sulphonamide. Ten days of sulphonamide treatment is as effective as 60 days, and both regimens seem to eliminate cystitis as well as pyelonephritis in almost all patients.⁸⁻⁹ Single-dose treatment is apparently equally effective, at least in treating infections of cystitis type.

Another advantage of the ultra-short treatment with short-acting sulphonamides is that the effect on the faecal flora seems to be slight, since there were few recurrences with sulphonamide-resistant strains. This contrasts with the results of a previous study performed on hospital patients, in which all early recurrences were resistant after 10 days of sulphonamide treatment.¹⁰ Further advantages are the low incidence of side effects and low cost.

Charlton *et al* showed that a three-day course of amoxicillin was as effective as a 10-day course¹¹ in uncomplicated UTIs in women. Women with infections confined to the bladder were cured with a single dose of kanamycin injected intramuscularly,¹² and single-dose treatment with amoxicillin has been successful in women with uncomplicated UTI.¹³⁻¹⁴ Amoxicillin and kanamycin are considered to be bactericidal agents. The present study shows that even a bacteriostatic agent, such as a short-acting sulphonamide, administered in a single dose is effective in children.

Single-dose treatment with ultra-long-acting sulphonamides effectively eliminates infection.¹⁵⁻¹⁶ One reason for the satisfactory results of this study with a short-acting sulphonamide may be that urinary concentrations of sulphafurazole remain at a therapeutic level for about 36 hours (Källenius and Dornbusch, unpublished observations). With this kind of benign UTI the urine concentration is probably more important than the serum concentration.

Ronald *et al*¹² found that failures with single-dose treatment were more common in infections affecting the kidney. One reason for this could be that pyelonephritic *E coli* strains are more able to adhere to human uroepithelial cells than strains confined to the bladder¹⁷ and thus may be more likely to survive in the urinary tract during short-term treatment. We found that the infecting strains in this study adhered well to human periurethral cells¹⁸ but a comparison with pyelonephritic strains might show quantitative differences. Prolonged prophylactic treatment may lessen the risk of further infections,¹⁹ so short-term treatment might increase the risk. In this study, however, there was no difference in the recurrence rate after single-dose treatment and treatment for 10 days or more.

We suggest that uncomplicated infections may safely and successfully be treated by a single oral dose of a short-acting sulphonamide.

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Requests for reprints should be addressed to: Dr G Källenius, Department of Paediatrics, Karolinska Hospital, S-104 01 Stockholm, Sweden.

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